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FILE 'HOME' ENTERED AT 09:44:23 ON 28 SEP 1999

=> index bioscience meetings

=> s stress protein and (CTL or cytotoxic (2w) lymphocyte) and antigen##

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L1    QUE STRESS PROTEIN AND (CTL OR CYTOTOXIC (2W) LYMPHOCYTE) AND ANTIGEN##

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scisearch


=> s l1; dup rem l2

L2          64 L1


PROCESSING COMPLETED FOR L2
L3           31 DUP REM L2 (33 DUPLICATES REMOVED)

=> d 1-31 bib ab


L3   ANSWER 1 OF 31  SCISEARCH  COPYRIGHT 1999 ISI (R)
AN   1999:628796  SCISEARCH
GA   The Genuine Article (R) Number: 224LH
TI   Intracellular rate-limiting steps in MHC class I antigen
     processing
AU   Montoya M; DelVal M (Reprint)
CS   INST SALUD CARLOS III, CTR NACL BIOL FUNDAMENTAL, CTRA POZUELO, KM 2,
     E-28220 MADRID, SPAIN (Reprint); INST SALUD CARLOS III, CTR NACL BIOL
     FUNDAMENTAL, E-28220 MADRID, SPAIN
CYA  SPAIN
SO   JOURNAL OF IMMUNOLOGY, (15 AUG 1999) Vol. 163, No. 4, pp. 1914-1922.
     Publisher: AMER ASSOC IMMUNOLOGISTS, 9650 ROCKVILLE PIKE, BETHESDA, MD
     20814.
     ISSN: 0022-1767.
DT   Article; Journal
FS   LIFE
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08/977,787

LA English.
REC Reference Count: 58
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Quantitative aspects of the endogenous pathway of Ag processing and presentation by MHC class I molecules to CD8(+) **CTL** were analyzed over a wide range of Ag expression in recombinant vaccinia virus-infected cells expressing beta-galactosidase as model Ag, Only the amount of starting Ag was varied, leaving other factors unaltered, Below a certain level of Ag synthesis, increasing protein amounts led to a sharp rise in recognition by **CTL**, Higher levels of Ag expression led to a saturation point, which intracellularly limited the number of naturally processed peptides bound to MHC and thereby also **CTL** recognition, The rate-limiting step was located at the binding of the **antigenic** peptide to MHC inside the vaccinia virus-infected cell or before this event.

L3 ANSWER 2 OF 31 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1999:391974 SCISEARCH
GA The Genuine Article (R) Number: 196MM
TI Truncated or chimeric endogenous protein **antigens** gain immunogenicity for B cells by **stress protein** -facilitated expression.
AU Schirmbeck R; Gerstner G; Reimann J (Reprint)
CS UNIV ULM, INST MED MICROBIOL, HELMHOLTZSTR 8-1, D-89081 ULM, GERMANY (Reprint); UNIV ULM, INST MED MICROBIOL, D-89081 ULM, GERMANY
CYA GERMANY
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (MAY 1999) Vol. 29, No. 5, pp. 1740-1749. Publisher: WILEY-V C H VERLAG GMBH, MUHLENSTRASSE 33-34, D-13187 BERLIN, GERMANY.
ISSN: 0014-2980.
DT Article; Journal
FS LIFE
LA English.
REC Reference Count: 30
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Truncated Variants of the SV40 large T **antigen** (T-Ag) with an intact N terminus are as efficiently expressed in eukaryotic transfectants as wild-type (wt) T-Ag. Coprecipitation of N-terminal T-Ag fragments with the constitutively expressed, cytosolic **stress protein** hsp73 suggests that this chaperone stabilized expression of the truncated T Ag fragments. In contrast to T-Ag, the 163-residue N-terminal preS domain of the hepatitis B surface **antigen** (HBsAg) is difficult to express. When the preS domain is C-terminally fused to a hsp73-binding cytoplasmic T-Ag (cT-Ag) fragment its stable expression as a chimeric cT-preS protein is obtained. DNA-based vaccination with plasmid DNA encoding either wt or hsp-associated mutant T-Ag elicited potent MHC class I-restricted, T-Ag-specific T cell responses. In contrast, DNA vaccination with hsp73-binding (mutant or chimeric) T-Ag variants, but not with wt T-Ag elicited T-Ag-specific antibody responses. Furthermore, vaccination with cT-preS-encoding plasmid DNA induced antibodies binding to the preS domain of the large HBsAg. Hence, hsp73-bound endogenous **antigens** efficiently stimulate antibody responses. These findings may be relevant for tumor immunology and autoimmunity.

L3 ANSWER 3 OF 31 SCISEARCH COPYRIGHT 1999 ISI (R)
AN 1999:198930 SCISEARCH
GA The Genuine Article (R) Number: 173EJ
TI Calreticulin, a peptide-binding chaperone of the endoplasmic reticulum, elicits tumor- and peptide-specific immunity
AU Basu S; Srivastava P K (Reprint)
CS UNIV CONNECTICUT, SCH MED, CTR IMMUNOTHERAPY CANC & INFECT DIS, MC1601, FARMINGTON, CT 06030 (Reprint); UNIV CONNECTICUT, SCH MED, CTR IMMUNOTHERAPY CANC & INFECT DIS, FARMINGTON, CT 06030
CYA USA
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1 MAR 1999) Vol. 189, No. 5, pp.

797-802.
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021.
ISSN: 0022-1007.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 28
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Calreticulin (CRT), a peptide-binding heat shock protein (HSP) of the endoplasmic reticulum (ER), has been shown previously to associate with peptides transported into the ER by transporter associated with **antigen** processing (Spee, P., and J. Neefjes. 1997. Eur. J. Immunol. 27: 2441-2449). Our studies show that CRT preparations purified from tumors elicit specific immunity to the tumor used as the source of CRT but not to all antigenically distinct tumor. The immunogenicity is attributed to the peptides associated with the CRT molecule and not to the CRT molecule per se. It is further shown that CRT molecules can be complexed in vitro to unglycosylated peptides and used to elicit peptide-specific CD8(+) T cell response in spite of exogenous administration. These characteristics of CRT closely resemble those of HSPs gp96, hsp90, and hsp70, although CRT has no apparent structural homologies to them.

L3 ANSWER 4 OF 31 MEDLINE DUPLICATE 1
AN 1999141650 MEDLINE
DN 99141650
TI Priming of CD8+ **CTL** effector cells in mice by immunization with a **stress protein**-influenza virus nucleoprotein fusion molecule.
AU Anthony L S; Wu H; Sweet H; Turnnir C; Roux L J; Mizzen L A
CS StressGen Biotechnologies Corporation, Victoria, BC, Canada..
lanthony@stressgen.com
SO VACCINE, (1999 Jan 26) 17 (4) 373-83.
Journal code: X60. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990702
AB Literature is accumulating which suggests the potential for stress proteins to form the basis of a novel vaccine technology. Immunization with mammalian tumor-derived stress proteins and their associated peptides promote anti-tumor immunity. Vaccination with HIV-1 p24 **antigen** fused to mycobacterial heat shock protein (Hsp) Hsp71 enhances p24 specific immunity, as measured by p24-specific antibody production and in vitro cell proliferation and cytokine induction. An ovalbumin-Hsp71 fusion protein primes ovalbumin-specific **CTL** activity and resistance to challenge with an ovalbumin-expressing tumor. We have extended these observations by using a mycobacterial Hsp65 fusion molecule to prime **CTL** specific for a viral **antigen**. Gene fusion constructs were generated from DNA encoding Mycobacterium bovis strain BCG Hsp65 and individual fragments of influenza virus nucleoprotein (NP) encompassing H-2Kd- and H-2Db-restricted **CTL** epitopes. The ability of these purified recombinant fusion proteins to prime NP-specific **CTL** was assessed in mice of appropriate H-2 haplotypes. We observed that adjuvant-free immunization with either fusion protein elicited significant **CTL** activity when administered at doses of 10-100 micrograms per mouse. An NP fusion protein made with glutathione-S-transferase failed to elicit NP-specific **CTL**, indicating that the phenomenon requires Hsp65 sequences. A single immunization with the Hsp65-NP fusion protein elicited **CTL** activity which persisted for a minimum of 4 months post-immunization, at which time it could be boosted by a second immunization. To our knowledge,

this is the first report of a member of the Hsp60 family priming for **antigen**-specific **CTL** activity when employed as a fusion protein partner.

L3 ANSWER 5 OF 31 CAPLUS COPYRIGHT 1999 ACS
AN 1999:131416 CAPLUS
DN 130:295186
TI Stress proteins and immunity mediated by cytotoxic T lymphocytes
AU Schild, Hansjorg; Arnold-Schild, Daniele; Lammert, Eckhard; Rammensee, Hans-Georg
CS Department of Immunology, Institute for Cell Biology, University of Tubingen, Tubingen, D-72076, Germany
SO Curr. Opin. Immunol. (1999), 11(1), 109-113.
CODEN: COPIEL; ISSN: 0952-7915
PB Current Biology Publications
DT Journal; General Review
LA English
AB A review with 55 refs. Chaperone mols., including members of the heat shock protein family, are able to stimulate .alpha..beta. and .gamma..delta. T cells as well as natural killer cells. For .alpha..beta. T cells, specificity is induced by chaperone-assisted peptides; this has lead to detailed investigations of peptides that bind to these chaperones and their possible role in **antigen** presentation.

L3 ANSWER 6 OF 31 CAPLUS COPYRIGHT 1999 ACS
AN 1998:388603 CAPLUS
DN 129:40131
TI Vaccines for inducing cell-mediated cytolytic response comprising **antigen** and **stress protein**
IN Mizzen, Lee; Anthony, Lawrence S. D.
PA Stressgen Biotechnologies Corp., Can.; Mizzen, Lee; Anthony, Lawrence S. D.
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9837899	A1	19980904	WO 1997-CA897	19971125
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851120	A1	19980622	AU 1998-51120	19971125
EP 941319	A1	19990915	EP 1997-945684	19971125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-756621 19961126
WO 1997-CA897 19971125
AB The present invention relates to a vaccine for inducing an immune response to an **antigen** in a vertebrate (e.g., mammal) comprising an **antigen** and all or a portion of a **stress protein** or all or a portion of a protein having an amino acid sequence sufficiently homologous to the amino acid sequence of the **stress protein** to induce the immune response against the **antigen**. In a particular embodiment, the present invention relates to vaccines and compns. which induce a **CTL** response in a mammal comprising an **antigen** and all or a portion of a **stress protein**. In another embodiment, the invention relates to vaccines and compns. which induce an immune response to an influenza virus in a

mammal comprising an **antigen** of the influenza virus and all or a portion of one or more stress proteins. The invention also relates to vaccines and compns. for inducing a **CTL** response to a tumor-assocd. **antigen** comprising a tumor-assocd. **antigen** and all or a portion of the **stress protein**. The invention also relates to vaccines and compn. for suppressing allergic immune responses to allergens comprising an allergen and all or a portion of a **stress protein**. Immunogens comprising influenza virus NP peptide and Mycobacterium hsp70, NP peptide-hsp70 conjugates and NP peptide-hsp70 fusion proteins were prepd. Mice immunized with these prepns. displayed a **CTL** response against cells exhibiting the NP peptide.

L3 ANSWER 7 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN 98A0996 JICST-EPlus
TI Proceeding of the 10th annual meeting of the Japanese Society of Biological Response Modifiers. Tumor-Derived Heat Shock Protein Chaperones Tumor-**Antigenic** Peptides.
AU HICUTA AKIO; ISHII TATSUAKI; MORIMOTO YOSHINORI; YAMANO TAKEHISA; FUJIWARA TOSHIYOSHI; UDONO HEIICHIRO; NAKAYAMA EIICHI; TANAKA NORIAKI
CS Okayama Univ., Sch. of Med.
SO Biotherapy (Tokyo), (1998) vol. 12, no. 5, pp. 573-575. Journal Code: L0028A (Ref. 3)
ISSN: 0914-2223
CY Japan
DT Journal; Short Communication
LA Japanese
STA New
AB Heat shock proteins(HSPs) facilitate intracellular translocation of **antigenic** peptides as chaperones and play an essential role in **antigen** processing and presentation. Tumor-derived HSPs function as tumor rejection **antigens** to induce tumor-specific transplantation resistance. To determine if tumor-derived HSPs chaperone tumor-**antigenic** peptides, we purified hsp70, gp96 and hsp90 from mouse radiation-induced leukemia RL 1 and dissociated peptides from the HSPs. Tandem mass spectrometry of the dissociated peptide fractions with which RL 1-specific **CTL**, Y-15 exhibited cytotoxicity agaist peptide-pulsed P815 revealed that hsp70 was associated with a known tumor-rejection-**antigenic** peptide, pRL1a, gp96 was associated with pRL1a and its precursor peptide, pRL1b, and hsp90 was associated with pRL1a, pRL1b and another unknown **antigenic** peptide. Hsp70 and gp96 purified from surgically resected human colon cancer strongly stimulated autologous peripheral blood mononuclear cells for the production of interferon .GAMMA., tumor necrosis factor .ALPHA. and proliferative responses. The cytotoxicity of tumor-specific cytotoxic T lymphocytes was also induced by the culture with the hsp70. These results suggest that the autologous cancer-derived HSP, which is associated with both known and unknown tumor-**antigenic** peptides, is an effective tumor vaccine for the immunotherapy of cancers without the HLA haplotype restriction. (author abst.)

L3 ANSWER 8 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN 98A0998 JICST-EPlus
TI Proceeding of the 10th annual meeting of the Japanese Society of Biological Response Modifiers. Possibility of In Vivo Therapy Using Tumor-**Antigen**-Derived Peptide.
AU YAMASAKI SEIJI; KANAOKA SHUNJI; INOUE NAOYA; OKINO TAKASHI; KAN NORIMICHI; SHIMADA YUTAKA; IMAMURA MASAYUKI
CS Kyoto Univ., Fac. of Med.
SO Biotherapy (Tokyo), (1998) vol. 12, no. 5, pp. 569-571. Journal Code: L0028A (Ref. 4)
ISSN: 0914-2223
CY Japan
DT Journal; Short Communication
LA Japanese

STA New
AB Using cultured dendritic cells(DCs) as **antigen** carriers, we compared tumor-**antigen**-derived peptide(s) with heat shock protein as peptide chaperones derived from tumor in a p53-mutated murine tumor model (Meth A fibrosarcoma syngeneic to BALB/c mouse) and MAGE-expressing esophageal or breast tumor in human. In Meth A tumor, heat shock protein-pulsed DCs were the most effective inducers for tumor-specific protection immunity. Using MAGE-3-derived and HLA-A2-restricted peptide (FLWGPPALV) with DCs, a peptide-specific **CTL** line was induced in a HLA-A2-positive long survivor from esophageal operation. This **CTL** line had 17% (E/T=40:1) of cytotoxicity against autologous esophageal tumor. In comparison with effectors from whole tumor lysate-pulsed DCs, the peptide-specific **CTL** line was less proliferative, less cytotoxic, but more specific against **antigen**-pulsed DC and autologous tumor. In a trial using whole tumor lysate-pulsed DCs against skin metastases from breast cancer (MAGE-1 and MAGE-3 positive), a direct antitumor response at the injected site was detected, but no immune responses using DTH response and CTLp frequency were detected. These results show that combination of several peptides and heat shock proteins with autologous DCs will be more immunogenic against in vivo heterogenous tumors than immunization with single peptide. (author abst.)

L3 ANSWER 9 OF 31 CAPLUS COPYRIGHT 1999 ACS
AN 1999:43518 CAPLUS
DN 130:290870
TI Priming of CD8+ **CTL** effector cells in mice by immunization with a **stress protein**-influenza virus nucleoprotein fusion molecule
AU Anthony, Lawrence S. D.; Wu, Huacheng; Sweet, Heather; Turnnir, Cor; Boux, Leslie J.; Mizzen, Lee A.
CS StressGen Biotechnologies Corporation, Victoria, BC, V8Z 4B9, Can.
SO Vaccine (1998), Volume Date 1999, 17(4), 373-383
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Literature is accumulating which suggests the potential for stress proteins to form the basis of a novel vaccine technol. Immunization with mammalian tumor-derived stress proteins and their assocd. peptides promote anti-tumor immunity. Vaccination with HIV-1 p24 **antigen** fused to mycobacterial heat shock protein (Hsp) Hsp71 enhances p24-specific immunity, as measured by p24-specific antibody prodn. and in vitro cell proliferation and cytokine induction. An ovalbumin-Hsp71 fusion protein primes ovalbumin-specific **CTL** activity and resistance to challenge with an ovalbumin-expressing tumor. The authors have extended these observations by using a mycobacterial Hsp65 fusion mol. to prime **CTL** specific for a viral **antigen**. Gene fusion constructs were generated from DNA encoding Mycobacterium bovis strain BCG Hsp65 and individual fragments of influenza virus nucleoprotein (NP) encompassing H-2Kd-and H-2Db-restricted **CTL** epitopes. The ability of these purified recombinant fusion proteins to prime NP-specific **CTL** was assessed in mice of appropriate H-2 haplotypes. The authors obsd. that adjuvant-free immunization with either fusion protein elicited significant **CTL** activity when administered at doses of 10-100 .mu.g per mouse. An NP fusion protein made with glutathione-S-transferase failed to elicit NP-specific **CTL**, indicating that the phenomenon requires Hsp65 sequences. A single immunization with the Hsp65-NP fusion protein elicited **CTL** activity which persisted for a min. of 4 mo post-immunization, at which time it could be boosted by a second immunization. To the authors' knowledge, this is the first report of a member of the Hsp60 family priming for **antigen**-specific **CTL** activity when employed as a fusion protein partner.

L3 ANSWER 10 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN 980235113 JICST-EPlus
TI The Mechanism of Escape from Anti-Tumor Immune Responses by Interleukin-10.
AU TSUKUMA TETSUHIRO; YAGIHASHI ATSUHITO; TORIGOE TOSHIHIKO; SATO NORIYUKI; KIFUCHI KOKICHI; HIRATA KOICHI
CS Sapporo Med. Coll., Sch. of Med.
SO Biotherapy (Tokyo), (1998) vol. 12, no. 1, pp. 44-47. Journal Code: L0028A
Fig. 4, Ref. 5
ISSN: 0914-2223
CY Japan
DT Journal; Article
LA Japanese
STA New
AB Tumor cells can escape the host's protective immune system, and the inhibitory cytokines have been reported to be involved in the mechanism of this escape. So we investigated the effects of IL-10 on tumor cells using WF1 cells which were the H-ras mediated transformant of WFB (a WKA rat fetusderived fibroblast cell line). We revealed that IL-10 downregulated the expression of the NK target structure(NKTS), reduced NK sensitivity, and downregulated the expression of MHC class I, which probably facilitated tumor cells' escape from the attack of the **CTL**. In addition, IL-10 downregulated the expression of heat shock protein which either 1), constituted a relay line in which the peptides were generated in the cytosol by the action of the proteases, until they were finally accepted by MHC class I molecules in the endoplasmic reticulum; or 2), bound to peptides that expressed themselves on the cell surface. These results suggest that IL-10 is involved in the mechanism by which the tumor cells escape from protective immune responses. (author abst.)

L3 ANSWER 11 OF 31 TOXLINE
AN 1999:58415 TOXLINE
DN CRISP-98-DK02259-05
TI HEAT SHOCK PROTEINS IN INTERSTITIAL NEPHRITIS.
AU WEISS R A
CS UNIVERSITY OF PENNSYLVANIA, 415 CURIE ROAD, PHILADELPHIA, PA 19104-6144 U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NAT INST OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.
NC 5R37DK02259-05
SO (1997). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
CY United States
DT (RESEARCH)
FS CRISP
LA English
EM 1998
AB ABSTRACT/CRISP My long term objectives applicable to this grant proposal are to define and characterize the immune mechanisms involved in toxin induced interstitial nephritis, and to develop therapeutic modalities to prevent disease progression in this important cause of chronic renal disease. Although studies in experimental autoimmune interstitial nephritis have defined and clarified many aspects of immune mediated interstitial injury, different target **antigens**, effector cells, accessory molecules and cytokines may play a role in toxin induced interstitial injury. The focus of this proposal is to further characterize the immune response directed against heat shock proteins in chronic cadmium-induced interstitial nephritis. Preliminary evidence suggests that cytotoxic CD4+ TCRalpha/beta bearing T cells that are HSP65 reactive mediate cytotoxic injury in this model. I plan to further characterize the expression of HSP70 and HSP65 and relevant cytokines and accessory molecules in this model. The molecular aspects of T cell response to endogenous renal HSP will be analyzed by defining Vbeta gene use in disease inducing T cell clones. Functional characteristics of cytotoxic T cell clones will be defined including their cytotoxic capacities in vitro and their ability to produce inflammatory infiltrates in the whole animal model. Finally, I plan to examine nephritic kidneys to characterize HSP reactive T cells in

kidneys with cadmium induced disease, and to culture and characterize T cell subsets defined in inflammatory infiltrates. Although it is beyond the scope of this current proposal, information gained from these studies will be used to develop strategies for treatment of toxin or stress induced interstitial nephritis.

L3 ANSWER 12 OF 31 MEDLINE DUPLICATE 2
AN 97439454 MEDLINE
DN 97439454
TI **Stress protein** (hsp73)-mediated, TAP-independent processing of endogenous, truncated SV40 large T **antigen** for Db-restricted peptide presentation.
AU Schirmbeck R; Bohm W; Reimann J
CS Institute for Medical Microbiology, University of Ulm, Germany.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Aug) 27 (8) 2016-23.
Journal code: EMS. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199711
EW 19971101
AB Transporter associated with **antigen** processing (TAP)-competent and TAP-deficient cell lines were transfected with expression plasmids encoding either the wild-type (wt) large tumor **antigen** (T-Ag) of SV40, or a truncated cytoplasmic variant (cT-Ag) of this viral protein. Stable expression of comparable levels of both forms of the viral protein was observed in different transfectants. The truncated cT-Ag variant, but not the wtT-Ag was stably associated with the constitutively expressed, cytosolic heat shock protein (hsp)73 chaperone. Two Db-binding peptides and one Kb-binding peptide of T-Ag were presented to **cytotoxic** T **lymphocyte** lines (CTLL) by TAP-competent transfectants expressing either wtT-Ag or cT-Ag. TAP-deficient transfectants expressing the wtT-Ag did not present any of these epitopes to CTLL. In contrast, TAP-deficient transfectants expressing the truncated hsp73-associated cT-Ag, presented the two Db-binding epitopes, but not the Kb-binding T-Ag epitope to CTLL. Resurgination of peptides by transfectants was not detectable. The described data indicate that a pool of post-Golgi Db molecules is available for 2-3 h in TAP-deficient transfectants for loading with peptides released during endolysosomal processing of hsp73-associated, endogenous **antigen**.

L3 ANSWER 13 OF 31 MEDLINE DUPLICATE 3
AN 97176459 MEDLINE
DN 97176459
TI The endoplasmic reticulum-resident **stress protein** gp96 binds peptides translocated by TAP.
AU Hammerl E; Arnold D; Nijenhuis M; Momburg F; Hammerling G J; Brunner J; Stevanovic S; Rammensee H G; Schild H
CS Department of Immunology, Institute for Cell Biology, University of Tubingen, Germany.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1997 Apr) 27 (4) 923-7.
Journal code: EMS. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199707
EW 19970704
AB The endoplasmic reticulum (ER)-resident **stress protein** gp96 induces a major histocompatibility complex class I-restricted **cytotoxic** T **lymphocyte** (**CTL**) response against **antigens** present in the cells from which it has been prepared. In this study, photoreactive peptides were translocated into the ER by the transporter associated with **antigen** processing (TAP). These

peptides can be cross-linked specifically to gp96. Thus, we provide the first evidence that gp96 binds TAP-translocated peptides which have been implicated in the induction of specific **CTL** responses after immunization with gp96 (Srivastava, P. K. et al., Immunogenetics 1994. 39: 93-).

L3 ANSWER 14 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN 970694462 JICST-EPlus
TI Heat Shock Cognate Protein 71-Associated Peptides Function as an Epitope for Toxoplasma gondii-Specific CD4+ **CTL**.
AU YANG T-H; AOSAI F; NOBOSE K; MUN H-S; YANO A
CS Chiba Univ. School of Medicine, Chiba, JPN
SO Microbiol Immunol, (1997) vol. 41, no. 7, pp. 553-561. Journal Code: F0715A (Fig. 4, Ref. 62)
ISSN: 0385-5600
CY Japan
DT Journal; Article
LA English
STA New
AB HLA-DR-restricted CD4+ **cytotoxic** T-**lymphocyte** (**CTL**) lines specific for Toxoplasma gondii (T. gondii)-infected melanoma cells have been established from peripheral blood lymphocytes (PBLs) of a patient with chronic toxoplasmosis. The role of heat shock cognate protein (HSC) 71 in **antigen** (Ag) processing and presentation of T. gondii-infected melanoma cells to these CD4+ **CTL** lines was investigated. A human melanoma cell line (P36) pulsed with T. gondii-infected P36 cell-derived HSC71 was lysed by a T. gondii-specific CD4+ **CTL** line (Tx-HSC-1). The Tx-HSC-1 also killed T. gondii-infected P36 cells. The lytic activity of Tx-HSC-1 against P36 cells pulsed with T. gondii-infected P36 cell-derived HSC71 was inhibited by monoclonal antibodies (mAbs) against HSC71. Anti-human leukocyte **antigen** (HLA)-DR mAb also partially blocked the lytic activity, whereas anti-HLA-A,B,C mAb did not block the lytic activity. In addition, a flow cytometric analysis with these specific mAbs against HSC71 showed HSC71 to be expressed on the cell surface of T. gondii-infected P36 cells as well as uninfected P36 cells. These data indicate that HSC71 molecules are expressed on human melanoma cell line P36, and that HSC71 may play a potential role in Ag presentation and processing of T. gondii-infected P36 cells to CD4+ **CTL**. (author abst.)

L2 ANSWER 15 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN 970700256 JICST-EPlus
TI Therapy for cancer. Identification and antitumor effect of tumor-rejection **antigen** peptide recognized by **CTL**.
AU NAKAYAMA EIICHI
CS Okayama Univ., Sch. of Med.
SO Monbusho Kagaku Kenkyuhi Hojokin ni yoru Gan Juten Kenkyu Hokoku Shuroku. Heisei 8 Nendo. Gan Kenkyu ni kakaru Juten Ryoiki Kenkyu, Gan Juten (Annual Report of the Research by Grant-in-Aid for Scientific Research on Priority Areas-Cancer- of Ministry of Education, Science and Culture), (1997) pp. 543-545. Journal Code: N199971654 (Ref. 6)
CY Japan
DT Journal; Short Communication
LA Japanese
STA New

L5 ANSWER 16 OF 31 MEDLINE DUPLICATE 4
AN 97388225 MEDLINE
DN 97388225
TI Influences of transporter associated with **antigen** processing (TAP) on the repertoire of peptides associated with the endoplasmic reticulum-resident **stress protein** gp96.
AU Arnold D; Wahl C; Faath S; Rammensee H G; Schild H
CS Department of Immunology, Institute of Cell Biology, Eberhard-Karls-

University, Tubingen, Germany.
SO JOURNAL OF EXPERIMENTAL MEDICINE, (1997 Aug 4) 186 (3) 461-6.
Journal code: I2V. ISSN: 0022-1007.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199710
EW 19971004
AB The endoplasmic reticulum (ER)-resident **stress protein** gp96 induces protective immunity and specific **cytotoxic** T **lymphocyte** (**CTL**) responses against **antigens** expressed in those cells it has been isolated from. This ability is based on peptides associated with gp96. Because gp96 is located inside the ER, our experiments address the question whether or not the repertoire of peptides associated with gp96 is influenced by the transporter associated with **antigen** processing (TAP). For this purpose, gp96 was isolated from cells with and without a TAP defect and used for immunization of mice. We found that for some **antigens** the association of peptides with gp96 required functional TAP molecules, whereas the association of peptides from other **antigens** was TAP independent. In the case of a TAP-dependent association of peptides with gp96, our results prove that peptide binding by gp96 in vivo occurs inside the ER and is not an artifact induced by cell lysis during the gp96 purification. The finding that some **antigens** can also associate with gp96 in the absence of functional TAP molecules indicates that the repertoire of peptides bound by gp96 truly reflects the entire repertoire of peptides present inside the ER and not only those peptides transported by TAP. These results, together with the earlier finding that the gp96 peptide repertoire is independent of the major histocompatibility complex molecules expressed by the cell gp96 is isolated from, give the theoretical foundation for the ability of gp96 to induce **CTL** responses against all kinds of intracellular **antigens**.

L8 ANSWER 17 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN [illegible] JICST-EPlus
TI The Population of Major Histocompatibility Complex(MHC) **Antigen** and Tumor Associated **Antigens**(TAAs) by Interleukin-10.
AU TSURUMA TETSUHIRO; YAGIHASHI ATSUHITO; TORIGOE TOSHIHIKO; SATO NORIYUKI; HIRATA KOICHI
CS Sapporo Med. Coll.
SO Sapporo Igaku Zasshi (Sapporo Medical Journal), (1997) vol. 66, no. 1/2, pp. 1-5. Journal Code: Z0302B (Fig. 6, Ref. 26)
ISSN: 0036-472X
CY Japan
DT Journal; Article
LA Japanese
STA New
AB Tumor cells can escape from the host's protective immune system: Natural Killer(NK) cells, **Cytotoxic** T cell **lymphocyte**(**CTL**), etc. The inhibitory cytokines, such as interleukin-4(IL-4), interleukin-10(IL-10), transforming growth factor-.BETA.(TGF-.BETA.), etc, have been reported to be involved in the mechanism of this escape. Although the effect of inhibitory cytokines on effector cells are well investigated, that on tumor cells is little known. We therefore investigated how IL-10 effects tumor cells using both W31 cells which were the H-ras mediated transformant of WFB (a WKA rat fetus-derived fibroblast cell line), and WMT-55, the polyoma middle T-mediated transformant of WFB. The above cells have Tumor Associated **Antigens**(TAAs), such as NK target structure(NKTS) and heat shock cognate(hsc), and are NK-sensitive. Cells were incubated for 3 days with rhIL-10 at different concentrations, and FACS analysis was performed. Then, following pretreatment of cells with rhIL-10 for 3 days, $^{51}Cr release assay was performed. In this study, we revealed that IL-10 downregulated the expression of the NK target structure, reduced NK sensitivity, and downregulated the expression of MHC

class I, which probably facilitated the tumor cells' escape from the attack of the **CTL**. In addition, IL-10 downregulated the expression of heat shock protein which either 1), constituted a relay line in which the peptides were generated in the cytosol by the action of the proteases, until they were finally accepted by MHC class I molecules in the endoplasmic reticulum; or 2), bound to peptides that expressed themselves on the cell surface. In other words, IL-10 downregulated the processing of peptides and the presentation of **antigens**. These effects of IL-10 are very important in an analysis of the mechanism by which the tumor cells escape from protective immune responses. (author abst.)

L3 ANSWER 18 OF 31 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96188173 EMBASE
DN 1996188173
TI Isolation of an immunodominant viral peptide that is endogenously bound to the **stress protein** GP96/GRP94.
AU Nieland T.J.F.; Tan M.C.A.A.; Monnee-Van Muijen M.; Koning F.; Kruisbeek A.M.; Van Bleek G.M.
CS Division of Immunology, Netherlands Cancer Institute,Amsterdam, Netherlands
SO Proceedings of the National Academy of Sciences of the United States of America, (1996) 93/12 (6135-6139).
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 004 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB Heat shock protein gp96 primes class I restricted cytotoxic T cells against **antigens** present in the cells from which it was isolated. Moreover, gp96 derived from certain tumors functions as an effective vaccine, causing complete tumor regressions in in vivo tumor challenge protocols. Because tumor-derived gp96 did not differ from gp96 isolated from normal tissues, a role for gp96 as a peptide carrier has been proposed. To test this hypothesis, we analyzed whether such an association of **antigenic** peptides with gp96 occurs in a well-defined viral model system. Here we present the full characterization of an **antigenic** peptide that endogenously associates with the **stress protein** gp96 in cells infected with vesicular stomatitis virus (VSV). This peptide is identical to the immunodominant peptide of VSV, which is also naturally presented by H-2Kb major histocompatibility complex class I molecules. This peptide associates with gp96 in VSV-infected cells regardless of the major histocompatibility complex haplotype of the cell. Our observations provide a biochemical basis for the vaccine function of gp96.

L3 ANSWER 19 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN 961017139 JICST-EPlus
TI Molecular Mechanisms for Cancer Immunity. Tumor Rejection Mechanism of Human Autologous Cancers.
AU SATO NORIYUKI; KIKUCHI KOICHI
CS Sapporo Med. Coll., Sch. of Med.
SO Biotherapy (Tokyo., (1996) vol. 10, no. 10, pp. 1295-1303. Journal Code: C0028A (Fig. 11, Tbl. 2, Ref. 7)
ISSN: 0914-7233
CY Japan
DT Journal; General Review
LA Japanese
STA New
AB Identification of **antigenic** peptides of tumors with clinically-high incidence, such as gastric cancers, is important for developing specific tumor vaccines. We established 10-15 systems of tumors and their **CTL** derived from various epithelial tissue origins,

and in this article the purification of **antigenic** peptide of gastric signet ring cell cancer HST-2 was described. The role and involvement of the molecular chaperones in the intracellular **antigen** processing of the peptide **antigens** were also described. (author abst.)

L3 ANSWER 20 OF 21 MEDLINE DUPLICATE 5
AN 96110144 MEDLINE
DN 96110144
TI Expression levels of **stress protein** gp96 are not limiting for major histocompatibility complex class I-restricted **antigen** presentation.
AU Lammert E; Arnold D; Rammensee H G; Schild H
CS Department of Tumorvirus Immunology, German Cancer Research Center, Heidelberg, Germany.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Apr) 26 (4) 875-9.
Journal code: ENS. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199608
AB Immunization of mice with gp96 induces **CTL** with specificity for proteins that are expressed in the cells from which gp96 was isolated (Arnold et al., J. Exp. Med. 1995. 182: 885, Udono et al., Proc. Natl. Acad. Sci. USA 1994. 91: 3077). Recently, it has been shown that gp96 from cells transfected with vesicular stomatitis virus (VSV) nucleocapsid protein as well as gp96 loaded in vitro with peptides containing an epitope of this protein are taken up by phagocytic cells which obtain thereby the capacity for stimulating VSV-specific cytotoxic T lymphocytes (Ciot and Srivastava, Science 1995. 269: 1585). The immunization experiments together with the peptide transfer from gp96-peptide complexes to major histocompatibility complex (MHC) class I molecules of phagocytic cells are consistent with the hypothesis that the endoplasmic reticulum-resident protein gp96 plays a crucial role in the **antigen** presentation of a cell (Srivastava et al., Immunogenetics 1994. 39: 93). To examine the involvement of gp96 in class I-restricted **antigen** presentation, we reduced gp96 RNA and protein levels by transfecting B16.1 cells with a vector containing part of gp96 cDNA in antisense orientation to the promotor. We found that antisense clones expressing strongly reduced levels of gp96 mRNA and gp96 protein show normal levels of MHC class I molecules on the cell surface and are recognized by T cells to the same extent as wild-type cells. Thus, our results show that normal levels of gp96 expression in a cell are not limiting for class I-restricted **antigen** presentation.

L3 ANSWER 21 OF 21 LIFESCI COPYRIGHT 1999 CSA
AN 96:107378 LIFESCI
TI Expression levels of **stress protein** gp96 are not limiting for major histocompatibility complex class I-restricted **antigen** presentation
AU Lammert, E.; Arnold, D.; Rammensee, H.-G.; Schild, H.*
CS Deutsches Krebsforschungszentrum, Abteilung Tumorvirus-Immunologie (0620), Im Neuenheimer Feld 242, D-69120 Heidelberg, FRG
SO EUR. J. IMMUNOL., (1996) vol. 116, no. 4, pp. 875-879.
ISSN: 0014-2980.
DT Journal
FS F
LA English
SL English
AB Immunization of mice with gp96 induces **CTL** with specificity for proteins that are expressed in the cells from which gp96 was isolated. Recently, it has been shown that gp96 from cells transfected with vesicular stomatitis virus (VSV) nucleocapsid protein as well as gp96 loaded in vitro with peptides containing an epitope of this protein are

taken up by phagocytic cells which obtain thereby the capacity for stimulating VSV-specific cytotoxic T lymphocytes. The immunization experiments together with the peptide transfer from gp96-peptide complexes to major histocompatibility complex (MHC) class I molecules of phagocytic cells are consistent with the hypothesis that the endoplasmic reticulum-resident protein gp96 plays a crucial role in the **antigen** presentation of a cell. To examine the involvement of gp96 in class I-restricted **antigen** presentation, we reduced gp96 RNA and protein levels by transfecting P13.1 cells with a vector containing part of gp96 cDNA in antisense orientation to the promotor. We found that antisense clones expressing strongly reduced levels of gp96 mRNA and gp96 protein show normal levels of MHC class I molecules on the cell surface and are recognized by T cells to the same extent as wild-type cells. Thus, our results show that normal levels of gp96 expression in a cell are not limiting for class I-restricted **antigen** presentation.

L4 ANSWER 22 OF 41 TOXLINE
AN 1996:[illegible]17 TOXLINE
DN CRISP-96-DK0[illegible]359-02
TI HEAT SHOCK PROTEINS IN INTERSTITIAL NEPHRITIS.
AU WELSH P A
CS UNIVERSITY OF PENNSYLVANIA, 422 CURIE BLVD, PHILADELPHIA, PA 19104-6144
U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NAT INST OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.
NC [illegible]-ADK[illegible]
SC [illegible] ; CRISP Data Base National Institutes Of Health. Award Type: G = Grant
CY United States
DT (RESEARCH)
FS CRISP
LA English
EM [illegible]
AB [illegible]: CRISP My long term objectives applicable to this grant proposal are to define and characterize the immune mechanisms involved in toxin induced interstitial nephritis, and to develop therapeutic modalities to prevent disease progression in this important cause of chronic renal disease. Although studies in experimental autoimmune interstitial nephritis have refined and clarified many aspects of immune mediated interstitial injury, different target **antigens**, effector cells, accessory molecules and cytokines may play a role in toxin induced interstitial injury. The focus of this proposal is to further characterize the immune response directed against heat shock proteins in chronic cadmium-induced interstitial nephritis. Preliminary evidence suggests that cytotoxic CD4+ TCRalphabeta bearing T cells that are HSP65 reactive mediate cytotoxic injury in this model. I plan to further characterize the expression of HSP70 and HSP65 and relevant cytokines and accessory molecules in this model. The molecular aspects of T cell response to endogenous renal HSP will be analyzed by defining Vbeta gene use in disease inducing T cell clones. Functional characteristics of cytotoxic T cell clones will be refined including their cytotoxic capacities in vitro and their ability to produce inflammatory infiltrates in the whole animal model. Finally, I plan to examine nephritic kidneys to characterize HSP reactive T cells in kidneys with cadmium induced disease, and to culture and characterize T cell subsets defined in inflammatory infiltrates. Although it is beyond the scope of this current proposal, information gained from these studies will be used to develop strategies for treatment of toxin or stress induced interstitial nephritis.

L3 ANSWER 23 OF 41 TOXLINE
AN 1996:[illegible]71 TOXLINE
DN CRISP-96-DK43351-050003
TI PILOT STUDY- HEAT SHOCK PROTEINS AND CYTOLYTIC T CELLS IN IBD.
AU MAGLER ANDERSON C
CS MASSACHUSETTS GENERAL HOSPITAL, FRUIT STREET, BOSTON, MA 0[illegible]14
U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NAT INST OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.

NC 5P30DK43251-050003
SO (1995). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
CY United States
DT (RESEARCH)
FS CRISP
LA English
EM 199504

L5 ANSWER 24 OF 31 JICST-EPlus COPYRIGHT 1999 JST
AN 960356619 JICST-EPlus
TI Tumor Rejection **Antigen** and Cancer Immunotherapy.
AU MATSUTAKE TOYOSHI; NAKAYAMA EIICHI
CS Okayama Univ., Sch. of Med.
SO Gan to Kagaku Ryoho (Japanese Journal of Cancer and Chemotherapy), (1995) vol. 22, no. 13, pp. 1871-1877. Journal Code: Z0938A (Ref. 37)
ISSN: 0385-0684
CY Japan
DT Journal; General Review
LA Japanese
STA New
AB Tumor rejection **antigen**(TRA) recognized by cytotoxic T cells(**CTL** have been identified on several murine tumors and human malignant melanomas. By utilizing these peptides as tumor vaccine, a new immunotherapy will be anticipated. Cancer cell vaccine and adoptive transfer of **CTL**/TIL have been undertaken successfully. Moreover, recombinant protein of tumor rejection **antigen** and heat shock protein emerge as promissing molecules as tumor **antigen**. To augument rather weak immune response, cytokine and gene therapies have now begun to be done. Cytokines can be used by themselves and also genes of cytokines can be introduced into either tumor cells or **CTL**/TIL. (author abst.)

L5 ANSWER 25 OF 31 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:148536 BIOSIS
DN PREV199598162536
TI Inhibition of autologous, tumor specific, gamma-delta, **cytotoxic** T **lymphocyte** (**CTL**) mediated cytolysis by anti-GRP75 antisera and characterization of a novel 69 kD cell surface protein.
AU Nelson, Edward L. (1); Naftzger, Clarissa; Welch, William J.; Clayberger, Carol; Krensky, Alan M.
CS (1) Lung Biology Cent., Univ. Calif. San Francisc, San Francisco, CA 94305 USA
SO Journal of Cellular Biochemistry Supplement, (1995) Vol. 0, No. 19B, pp. 231.
Meeting Info.: Keystone Symposium on Heat Shock (Stress) Proteins in Biology and Medicine Santa Fe, New Mexico, USA February 27-March 5, 1995
ISSN: 0733-1959.
DT Conference
LA English

L5 ANSWER 26 OF 31 TOXLINE
AN 1995:207175 TOXLINE
DN CRISP-95-DK43251-01A1
TI HEAT SHOCK PROTEINS IN INTERSTITIAL NEPHRITIS.
AU WEISS R A
CS UNIVERSITY OF PENNSYLVANIA, 422 CURIE BLVD, PHILADELPHIA, PA 19104-6144
U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NAT INST OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.
NC 1RO1DK01259-01A1
SO (1994). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
CY United States
DT (RESEARCH)
FS CRISP

LA English
EM 199507
AB PROJ/CRISP My long term objectives applicable to this grant proposal are to define and characterize the immune mechanisms involved in toxin induced interstitial nephritis, and to develop therapeutic modalities to prevent disease progression in this important cause of chronic renal disease. Although studies in experimental autoimmune interstitial nephritis have defined and clarified many aspects of immune mediated interstitial injury, different target **antigens**, effector cells, accessory molecules and cytokines may play a role in toxin induced interstitial injury. The focus of this proposal is to further characterize the immune response directed against heat shock proteins in chronic cadmium-induced interstitial nephritis. Preliminary evidence suggests that cytotoxic CD4+ TCRalpha/beta bearing T cells that are HSP65 reactive mediate cytotoxic injury in this model. I plan to further characterize the expression of HSP70 and HSP65 and relevant cytokines and accessory molecules in this model. The molecular aspects of T cell response to endogenous renal HSP will be analyzed by defining V beta gene use in disease inducing T cell clones. Functional characteristics of cytotoxic T cell clones will be defined including their cytotoxic capacities in vitro and their ability to produce inflammatory infiltrates in the whole animal model. Finally, I plan to examine nephritic kidneys to characterize HSP reactive T cells in kidneys with cadmium induced disease, and to culture and characterize T cell subsets defined in inflammatory infiltrates. Although it is beyond the scope of this current proposal, information gained from these studies will be used to develop strategies for treatment of toxin or stress induced interstitial nephritis.

L3 ANSWER 7 OF 31 TOXLINE
AN [illegible] TOXLINE
DN CRISP-94-DK43351-04C003
TI PILOT STUDY--HEAT SHOCK PROTEINS AND CYTOLYTIC T CELLS IN IBD.
AU MACKER-ANDERSON C
CS MASSACHUSETTS GENERAL HOSPITAL, FRUIT STREET, BOSTON, MA 02114
U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NAT INST OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.
NC 5R01DK43351-04C003
SO 1994. Crisp Data Base National Institutes Of Health. Award Type: G = Grant
CY United States
DT RESEARCH)
FS CRISP
LA English
EM 199507

L3 ANSWER 26 OF 31 MEDLINE DUPLICATE 6
AN 94298844 MEDLINE
DN 94298844
TI Peptide transporter-independent, **stress protein** -mediated endosomal processing of endogenous protein **antigens** for major histocompatibility complex class I presentation.
AU Schirmbeck R; Reimann J
CS Institute for Microbiology, University of Ulm, FRG.
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1994 Jul) 24 (7) 1478-86.
Journal code: EMS. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199410
AB The peptide transporter-defective cell line RMA-S expressing the wild-type simian virus 40 large T **antigen** (wtT-Ag) from a transfected gene did not present two well-defined, H-2 class I (Db)-restricted epitopes of T-Ag to cytotoxic T lymphocytes (**CTL**). Hence, "endogenous" processing and presentation of the wtT-Ag depended on a functional peptide transporter heterodimer. In contrast, both T-Ag epitopes were efficiently

presented to **CTL** by transfected RMA-S cells expressing a truncated, cytoplasmic T-Ag variant (cT-Ag) or a karyophilic, amino-terminal 272-amino acid T-Ag fragment. Transporter-independent "endogenous" processing of mutant T-Ag molecules correlated with their association with the constitutively expressed heat shock protein 73 (hsp73). Class I-restricted presentation of both epitopes processed from these hsp73-associated protein **antigens** was sensitive to NH4Cl and chloroquine. These data indicate that selected intracellular proteins access an alternative, hsp73-mediated pathway for class I-restricted presentation that operates independent of peptide transporters in an endosomal compartment.

L3 ANSWER 29 OF 31 TOXLINE
AN 1994:56850 TOXLINE
DN CRISP-94-DK43851-020002
TI PILOT STUDY--HEAT SHOCK PROTEINS AND CYTOLYTIC T CELLS IN IBD.
AU NAGLER-ANDERSON C
CS MASSACHUSETTS GENERAL HOSPITAL, FRUIT STREET, BOSTON, MA 02114
U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NAT INST OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.
NC 5P50DK43851-02;0003
SO (1993). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
CY United States
DT (RESEARCH)
FS CRISP
LA English
EM 199403

L3 ANSWER 30 OF 31 EMBASE COPYRIGHT 1994 ELSEVIER SCI. B.V.
AN 94014046 EMBASE
DN 1994014046
TI Suppression of **stress protein** GRP78 induction in tumor B/C10ME eliminates resistance to cell mediated cytotoxicity.
AU Sugawara S.; Takeda K.; Lee A.; Dennert G.
CS Department of Microbiology, University of Southern California,Los Angeles, CA 90033-0800, United States
SO Cancer Research, (1993) 53/24 (6001-6005).
ISSN: 0008-5472 CODEN: CNREA8
CY United States
DT Journal; Article
FS 016 Cancer
LA English
SL English
AB Tumor cells undergo self-destruction when incubated with cytotoxic T-cells (**CTL**) consistent with the observation that suppression of target protein synthesis causes resistance to apoptosis. Resistance to **CTL** is also induced by stress, suggesting that pathways exist suppressing apoptosis. Here we examine whether stress induced lysis resistance to **CTL** and tumor necrosis factor .alpha. involves stress proteins GRP78 and GRP94. We show that inhibition of GRP78 synthesis by transfection of cells with grp78 antisense vector pRSV- 78WO leads to inability to induce resistance to **CTL** or tumor necrosis factor .alpha.. Resistance induced in untransfected cells is reversible upon stress removal and correlates with GRP78 rephosphorylation, consistent with the notion that phosphorylated GRP78 is nonfunctional. The possibility that GRP78 plays a role in defense against **CTL** mediated apoptosis is supported by the finding that **CTL** but not CD4+ cells express a high level of unphosphorylated GRP78.

L3 ANSWER 31 OF 31 TOXLINE
AN 1994:56849 TOXLINE
DN CRISP-94-DK43851-020003
TI PILOT STUDY--HEAT SHOCK PROTEINS AND CYTOLYTIC T CELLS IN IBD.
AU NAGLER-ANDERSON C

CS MASSACHUSETTS GENERAL HOSPITAL, FRUIT STREET, BOSTON, MA 02114
    U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL
    INST. OF HEALTH, NAT INST OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES.
NC 5P30DK43351-020003
SO (1992). Crisp Data Base National Institutes Of Health. Award Type: G =
    Grant
CY United States
DT (RESEARCH)
FS CRISP
LA English
EM 199403

=> index biosscience meetings

=> s (hsp65 or hsp71) and influenza and antigen##

          1 FILE ADISINSIGHT
          1 FILE AIDSLINE
          4 FILE BIOSIS
          1 FILE BIOTECHABS
          2 FILE BIOTECHDS
          5 FILE CAPLUS
          2 FILE CIN
  19 FILES SEARCHED...
         10 FILE DGENE
          2 FILE DPCGNL
          2 FILE DRUGU
          5 FILE EMBASE
          1 FILE ESBIOBASE
  49 FILES SEARCHED...
          2 FILE LIFESCI
          5 FILE MEDLINE
          1 FILE PROMT
          5 FILE SCISEARCH
          2 FILE USPATFULL
          1 FILE WPIDS
          1 FILE WPINDEX

  19 FILES HAVE ONE OR MORE ANSWERS,   66 FILES SEARCHED IN STNINDEX

L4   QUE (HSP65 OR HSP71) AND INFLUENZA AND ANTIGEN##

=> file medline aidsline biosis caplus cancerlit embase jicst-eplus lifesci toxline
scisearch

=> s l4; dup rem l5

L5   27 L4

PROCESSING COMPLETED FOR L5
L6   8 DUP REM L5 (19 DUPLICATES REMOVED)

=> d 1-8 bib ab

L6   ANSWER 1 OF 8 MEDLINE   DUPLICATE 1
AN   1999141650   MEDLINE
DN   99141650
TI   Priming of CD8+ CTL effector cells in mice by immunization with a stress
     protein-**influenza** virus nucleoprotein fusion molecule.
AU   Anthony L S; Wu H; Sweet H; Turnnir C; Boux L J; Mizzen L A
CS   StressGen Biotechnologies Corporation, Victoria, BC, Canada..
     lanthony@stressgen.com

SO VACCINE, (1999 Jan 28) 17 (4) 373-83.
Journal code: X60. ISSN: 0264-410X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990708
AB Literature is accumulating which suggests the potential for stress proteins to form the basis of a novel vaccine technology. Immunization with mammalian tumor-derived stress proteins and their associated peptides promote anti-tumor immunity. Vaccination with HIV-1 p24 **antigen** fused to mycobacterial heat shock protein (Hsp) **Hsp71** enhances p24-specific immunity, as measured by p24-specific antibody production and in vitro cell proliferation and cytokine induction. An ovalbumin-**Hsp71** fusion protein primes ovalbumin-specific CTL activity and resistance to challenge with an ovalbumin-expressing tumor. We have extended these observations by using a mycobacterial **Hsp65** fusion molecule to prime CTL specific for a viral **antigen**. Gene fusion constructs were generated from DNA encoding Mycobacterium bovis strain BCG **Hsp65** and individual fragments of **influenza** virus nucleoprotein (NP) encompassing H-2Kd- and H-2Db-restricted CTL epitopes. The ability of these purified recombinant fusion proteins to prime NP-specific CTL was assessed in mice of appropriate H-2 haplotypes. We observed that adjuvant-free immunization with either fusion protein elicited significant CTL activity when administered at doses of 10-100 micrograms per mouse. An NP fusion protein made with glutathione-S-transferase failed to elicit NP-specific CTL, indicating that the phenomenon requires **Hsp65** sequences. A single immunization with the **Hsp65**-NP fusion protein elicited CTL activity which persisted for a minimum of 4 months post-immunization, at which time it could be boosted by a second immunization. To our knowledge, this is the first report of a member of the Hsp60 family priming for **antigen** -specific CTL activity when employed as a fusion protein partner.

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 1999 ACS
AN 1998:889602 CAPLUS
DN 130:40131
TI Vaccines for inducing cell-mediated cytolytic response comprising **antigen** and stress protein
IN Mizzen, Lee; Anthony, Lawrence S. D.
PA Stressgen Biotechnologies Corp., Can.; Mizzen, Lee; Anthony, Lawrence S. D.
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9837385	A1	19980604	WO 1997-CA897	19971125
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, CW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851120	A1	19980622	AU 1998-51120	19971125
EP 941319	A1	19990915	EP 1997-945684	19971125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1996-760621		19961126		
WO 1997-CA897		19971125		

AB The present invention relates to a vaccine for inducing an immune response to an **antigen** in a vertebrate (e.g., mammal) comprising an **antigen** and all or a portion of a stress protein or all or a portion of a protein having an amino acid sequence sufficiently homologous to the amino acid sequence of the stress protein to induce the immune response against the **antigen**. In a particular embodiment, the present invention relates to vaccines and compns. which induce a CTL response in a mammal comprising an **antigen** and all or a portion of a stress protein. In another embodiment, the invention relates to vaccines and compns. which induce an immune response to an **influenza** virus in a mammal comprising an **antigen** of the **influenza** virus and all or a portion of one or more stress proteins. The invention also relates to vaccines and compns. for inducing a CTL response to a tumor-assocd. **antigen** comprising a tumor-assocd. **antigen** and all or a portion of the stress protein. The invention also relates to vaccines and compn. for suppressing allergic immune responses to allergens comprising an allergen and all or a portion of a stress protein. Immunogens comprising **influenza** virus NP peptide and Mycobacterium hsp70, NP peptide-hsp70 conjugates and NP peptide-hsp70 fusion proteins were prepd. Mice immunized with these prepns. displayed a CTL response against cells exhibiting the NP peptide.

L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 1999 ACS
AN 1999:43518 CAPLUS
DN 130:250870
TI Priming of CD8+ CTL effector cells in mice by immunization with a stress protein-**influenza** virus nucleoprotein fusion molecule
AU Anthony, Lawrence S. D.; Wu, Huacheng; Sweet, Heather; Turnnir, Cir; Boux, Leslie J.; Mizzen, Lee A.
CS StressGen Biotechnologies Corporation, Victoria, BC, V8Z 4B9, Can.
SO Vaccine (1998), Volume Date 1999, 17(4), 373-383
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Literature is accumulating which suggests the potential for stress proteins to form the basis of a novel vaccine technol. Immunization with mammalian tumor-derived stress proteins and their assocd. peptides promote anti tumor immunity. Vaccination with HIV-1 p24 **antigen** fused to mycobacterial heat shock protein (Hsp) **Hsp71** enhances p24-specific immunity, as measured by p24-specific antibody prodn. and in vitro cell proliferation and cytokine induction. An ovalbumin-**Hsp71** fusion protein primes ovalbumin-specific CTL activity and resistance to challenge with an ovalbumin-expressing tumor. The authors have extended these observations by using a mycobacterial **Hsp65** fusion mol. to prime CTL specific for a viral **antigen**. Gene fusion constructs were generated from DNA encoding Mycobacterium bovis strain BCG **Hsp65** and individual fragments of **influenza** virus nucleoprotein (NP) encompassing H-2Kd-and H-2Db-restricted CTL epitopes. The ability of these purified recombinant fusion proteins to prime NP-specific CTL was assessed in mice of appropriate H-2 haplotypes. The authors obsd. that adjuvant-free immunization with either fusion protein elicited significant CTL activity when administered at doses of 10-100 .mu.g per mouse. An NP fusion protein made with glutathione-S-transferase failed to elicit NP-specific CTL, indicating that the phenomenon requires **Hsp65** sequences. A single immunization with the **Hsp65**-NP fusion protein elicited CTL activity which persisted for a min. of 4 mo post-immunization, at which time it could be boosted by a second immunization. To the authors' knowledge, this is the first report of a member of the Hsp60 family priming for **antigen**-specific CTL activity when employed as a fusion protein partner.

L6 ANSWER 4 OF 8 MEDLINE DUPLICATE 2
AN 95172747 MEDLINE
DN 95172747
TI Synthetic peptides representing T-cell epitopes act as carriers in pneumococcal polysaccharide conjugate vaccines.
AU de Velasco E A; Merkus D; Anderton S; Verheul A F; Lizzio E F; Van der Zee R; Van Eden W; Hoffman T; Verhoef J; Snippe H
CS Eijkman-Winkler Institute for Medical and Clinical Microbiology, Utrecht University, The Netherlands..
SO INFECTION AND IMMUNITY, (1995 Mar) 63 (3) 961-8.
Journal code: GC7. ISSN: 0019-9567.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199506
AB Improvement of antibody responses to polysaccharides through their linkage to proteins is thought to be mediated by protein-specific T helper (Th) cells. To investigate whether the carrier protein of a conjugate could be substituted by a Th epitope, Streptococcus pneumoniae type 17F polysaccharide (PS) was bromoacetylated and coupled to different peptides via their carboxy-terminal cysteines. Two peptides, one from the mycobacterial 65-kDa heat shock protein (**hsp65**) and the other from **influenza** virus hemagglutinin, are well-known Th epitopes. Two other peptides were selected from the pneumolysin sequence by Th epitope prediction methods; one of them was synthesized with cysteine either at the carboxy or the amino terminus. Three conjugates consistently elicited in mice anti-PS immunoglobulin M (IgM) and IgG responses that were not observed upon immunization with derivatized PS without peptide. The same conjugates induced no anti-PS antibody responses in athymic (nu/nu) mice, whereas clear responses were elicited in euthymic (nu/+) controls, demonstrating the thymus-dependent character of these conjugates. Only the three conjugates inducing anti-PS responses were capable of eliciting antipeptide antibodies. One of the immunogenic conjugates was studied in more detail. It induced significant protection and an anti-PS IgG response comprising all subclasses. On the basis of these results and proliferation studies with peptide and conjugate-primed cells, it is concluded that linkage of Th epitopes to PS in the right orientation enhances its immunogenicity in a thymus-dependent manner. Future possibilities for using peptides as carriers for inducing antibody responses to poorly immunogenic saccharide **antigens** are discussed.

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 1999 ACS
AN 1995:460155 CAPLUS
DN 122:237199
TI Microvariation creates significant functional differences in the DR3 molecules
AU Busch, Phillip E.; Araujo, Hugo A.; Creswell, Karen; Praud, Chantal; Johnson, Armead H.; Hurley, Carolyn Katovich
CS Department Microbiology and Immunology, Georgetown University Medical Center, Washington, DC, USA
SO Hum. Immunol. (1995), 42(1), 61-71
CODEN: HUIMDQ; ISSN: 0198-8859
DT Journal
LA English
AB Two DR3 mols. differ by four amino acids whose side chains point into the DR **antigen**-binding groove. To begin to assess the role of microvariation on DR3 function, DRB1*0302 residues were replaced with DRB1*0301 residues at .beta.-chain positions 26, 47, 86, and 47 plus 86. Murine fibroblast cell lines expressing DR(.alpha.,.beta.1*0301), DR(.alpha.,.beta.1*0302), and the four mutant 0302 mols. were examd. for alloproliferative DR(.alpha.,.beta.1*0302)-specific TLC stimulation and peptide binding. Changing position 26 had the most profound effect on T-cell recognition (seven of nine TLCs did not respond). Two TLCs did not respond to the mutant 0302V86 mol. and four TLCs that did respond to this

mutant lost responsiveness when positions 47 and 86 were mutated together. These data suggest that each of these variant residues, including position 47, influence T-cell recognition. Surprisingly, none of the mutations had an effect on the abs. binding of HA 307-319 (DR[.alpha.,.beta.1*0302] specific) and HSP 3-13 (DR[.alpha.,.beta.1*0301] specific); however, the mutant 0302 mols. changed at position 86 (glycine to valine) consistently bound HA 307-319 at significantly higher levels than DR[.alpha.,.beta.1*0301]. These data for position 86 are in contrast to other DR mols. and indicate that peptide contact residues for a specific DR mol. cannot be predicted based on binding results obtained with other DR mols. These data suggest that each of these variant groove residues, although not accessible to the TCR, contribute to the significant functional differences between the DR3 microvariants through subtle influences on the DR3-peptide complex.

L6 ANSWER 6 OF 8 MEDLINE DUPLICATE 3
AN 94046864 MEDLINE
DN 94046864
TI Responses to gram-negative enteric bacterial **antigens** by synovial T cells from patients with juvenile chronic arthritis: recognition of heat shock protein HSP60.
AU Life P; Hassell A; Williams K; Young S; Bacon P; Southwood T; Gaston J S
CS Department of Rheumatology, Birmingham University, UK..
SO JOURNAL OF RHEUMATOLOGY, (1993 Aug) 20 (8) 1388-96.
Journal code: JWX. ISSN: 0315-162X.
CY Canada
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199402
AB OBJECTIVE. To investigate the **antigenic** specificity of synovial T cells in juvenile chronic arthritis (JCA). METHODS. Synovial fluid and peripheral blood mononuclear cells from 24 patients with JCA were tested for their proliferative responses to recall **antigens**, enteric organisms associated with reactive arthritis, **influenza** A and a recombinant preparation of a mycobacterial heat shock protein, **HSP65**. To investigate further recognition of this last **antigen**, synovial T cells from one B27+ patient with pauciarticular disease were cloned using **HSP65**. The specificity of the resultant clones was then examined. RESULTS. Marked synovial T cell responses to enteric organisms and to **HSP65** were noted, particularly in HLA-B27+, pauciarticular patients; these were similar to those seen in a B27+ patient with reactive arthritis. Responses to enteric organisms and to **HSP65** were significantly correlated, suggesting recognition of an epitope common to these **antigen** preparations. However, all of the T cell clones obtained using **HSP65** proved to recognize E. coli derived **antigens** contaminating the recombinant **HSP65** rather than the mycobacterial **antigen**; these contaminants included the 60 kDa E. coli HSP, GroEL. The GroEL specific T cells did not respond to heat shocked human cells; this suggests (but does not prove) that they do not crossreact with human HSP60. CONCLUSION. Synovial T cell recognition of **antigens** from enteric organisms associated with reactive arthritis is a common feature in pauciarticular JCA. Among the target **antigens** is the GroEL HSP, but T cells recognizing this **antigen** do not necessarily crossreact with the homologous human HSP60.

L6 ANSWER 7 OF 8 MEDLINE DUPLICATE 4
AN 93360929 MEDLINE
DN 93360929
TI **hsp65** mRNA+ macrophages and gamma delta T cells in **influenza** virus-infected mice depleted of the CD4+ and CD8+ lymphocyte subsets.
AU Allan W; Tabi Z; Lukacs K; Doherty P C
CS Department of Immunology, St Jude Children's Research Hospital, Memphis,

TN 38105.
NC AI 29579 (NIAID)
SO MICROBIAL PATHOGENESIS, (1993 Jan) 14 (1) 75-84.
Journal code: MIC. ISSN: 0882-4010.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199310
AB The effects of depleting CD4+ and CD8+ T cells on macrophage recruitment have been analyzed for bronchoalveolar lavage (BAL) populations from mice with primary or secondary **influenza** pneumonia. Macrophages were characterized by both the capacity to engulf latex particles and the expression of mRNA for a 65 kD heat shock protein (**hsp65**). The localization of **hsp65** mRNA+ cells to the pneumonic lung was greatly enhanced in the secondary response. Eliminating the CD4+ and CD8+ T cells decreased the prevalence of **hsp65** mRNA+latex+ macrophages as much as seven-fold, though the frequency of latex+ cells was higher in the residual inflammatory process. The CD4-8- gamma delta T cells were also relatively enriched in the BAL from the depleted mice. However, the localization of gamma delta T cells to the pneumonic lung does not compensate either quantitatively or qualitatively for the lack of the CD4+ and CD8+ alpha beta T-cell subsets, which are responsible for activating a substantial proportion of the phagocytic cells to express transcripts of an endogenous **hsp65** gene.

L6 ANSWER 5 OF 8 MEDLINE DUPLICATE 5
AN 92111612 MEDLINE
DN 92111612
TI binding of a major T cell epitope of mycobacteria to a specific pocket within HLA-DRw17(DR3) molecules.
AU Geluk A; Bloemhoff W; De Vries R R; Ottenhoff T H
CS Department of Immunohematology and Blood Bank, University Hospital, Leiden, The Netherlands..
SO EUROPEAN JOURNAL OF IMMUNOLOGY, (1992 Jan) 22 (1) 197-13.
Journal code: EMS. ISSN: 0014-2980.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199204
AB CD4+ T cells recognize **antigenic** peptides bound to the polymorphic peptide-binding site of major histocompatibility complex (MHC) class II molecules. The polymorphism of this site is thought to dictate which peptides can be bound and thus presented to the T cell receptor. The mycobacterial 65-kDa heat-shock protein (**hsp65**) peptide 3-13 is an important T cell epitope: it is immunodominant in the mycobacterium-specific T cell response of HLA-DR3+ individuals but, interestingly cannot be recognized in the context of any other HLA-DR molecules. We, therefore, have tested whether the **hsp65** epitope p3-13 is selected for T cell recognition in the context of only HLA-DR3 molecules by an unique binding specificity for HLA-DR3. Using biotinylated peptides and EBV-transformed BLCL comprising all known HLA class II specificities, we find that p3-13 binds to HLA-DRw17(DR3) but not to any other HLA-DR molecule. Conversely, a control peptide p307-319 **influenza** hemagglutinin binds to all known HLA-DR molecules but only weakly to HLA-DRw17 and HLA-DR9. Peptide binding could be inhibited by excess unbiotinylated competitor analogue as well as by anti-DR monoclonal antibodies but not by anti-class I-, anti-DP- or anti-DQ monoclonal antibodies. The amino acid sequence of DRw17 molecules differs uniquely at five positions from the other DR beta 1 sequences. Three of these five residues (positions 26, 71 and 74) are potential peptide contacting residues. These residues map closely together in the hypothetical three-dimensional model of the DR molecule and, thus, most probably form a positively charged pocket, critical for the binding of

p3-13. Interestingly, p3-13 does not bind to a DR3 variant, the DRw18 molecule. The DRw18 beta 1 chain differs from DRw17 at two major positions, close to or within the DRw17-specific pocket. These substitutions drastically change the structure and charge of the pocket and thus presumably abrogate its ability to bind p3-13.

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